Clinical trial results:
A Multicentre, Randomised, Double-blind, Placebo-Controlled Phase III Extension Study to Characterise the Long-term Safety and Tolerability of Anifrolumab in Adult Patients with Active Systemic Lupus Erythematosus

Summary

EudraCT number	2016-000625-39
Trial protocol	HU DE ES LT BG
Global end of trial date	21 December 2021

Results information

Result version number	v1 (current)
This version publication date	04 January 2023
First version publication date	04 January 2023

Trial information

Trial identification

Sponsor protocol code	D3461C00009

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02794285
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Astraalléen, Södertälje, Sweden, SE-151 85
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 December 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to characterise the long-term safety and tolerability of intravenous (IV) anifrolumab.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Conference of Harmonisation/Good Clinical Practice, applicable regulatory requirements and the AstraZeneca policy on Bioethics.

Background therapy:

Whereas the background standard of care had to remain stable throughout Phase III feeder studies (D3461C00004 [NCT02446899] or D3461C00005 [NCT02446912]). Investigators were allowed to change dose or add new background immunosuppressants as clinically indicated (with certain exceptions e.g., cyclophosphamide and other biologics that were not permitted). In addition, oral corticosteroid (OCS) and antimalarials could be changed.

Evidence for comparator: -

Actual start date of recruitment	30 June 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 9
Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Chile: 7
Country: Number of subjects enrolled	Colombia: 4
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Japan: 33
Country: Number of subjects enrolled	Lithuania: 18
Country: Number of subjects enrolled	Mexico: 29
Country: Number of subjects enrolled	Peru: 22
Country: Number of subjects enrolled	Poland: 52
Country: Number of subjects enrolled	Romania: 20

Country: Number of subjects enrolled	Russian Federation: 14
Country: Number of subjects enrolled	South Africa: 8
Country: Number of subjects enrolled	Korea, Republic of: 12
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Taiwan: 9
Country: Number of subjects enrolled	Ukraine: 25
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	United States: 203
Worldwide total number of subjects	547
EEA total number of subjects	143

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	530
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This long-term extension (LTE) study was conducted at 176 study centres in 24 countries.

Pre-assignment

Screening details:

The LTE population was comprised of participants who had completed the 52-week double-blind treatment period in one of the Phase III feeder studies (D3461C00004 [NCT02446899] or D3461C00005 [NCT02446912]), met all LTE eligibility criteria, and were willing to continue into the extension study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Randomised Anifrolumab 300 mg

Arm description:

Anifrolumab (300 mg) administered via an intravenous (IV) infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered anifrolumab (300 mg) in a feeder study.

Arm type	Experimental
Investigational medicinal product name	Anifrolumab
Investigational medicinal product code	MEDI-546
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as an IV infusion via an infusion pump over a minimum of 30 minutes.

Arm title	Placebo Feeder + Placebo LTE

Arm description:

Placebo administered via an IV infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered placebo in a feeder study.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as an IV infusion via an infusion pump over a minimum of 30 minutes.

Arm title	Placebo Feeder + Anifrolumab 300 mg LTE

Arm description:

Anifrolumab (300 mg) administered via an IV infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered placebo in a feeder study.

Arm type	Experimental

Investigational medicinal product name	Anifrolumab
Investigational medicinal product code	MEDI-546
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as an IV infusion via an infusion pump over a minimum of 30 minutes.

Arm title	Anifrolumab 150 mg Feeder + Anifrolumab 300 mg LTE

Arm description:

Anifrolumab (300 mg) administered via an IV infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered anifrolumab (150 mg) in a feeder study.

Arm type	Experimental
Investigational medicinal product name	Anifrolumab
Investigational medicinal product code	MEDI-546
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as an IV infusion via an infusion pump over a minimum of 30 minutes.

Number of subjects in period 1	Randomised Anifrolumab 300 mg	Placebo Feeder + Placebo LTE	Placebo Feeder + Anifrolumab 300 mg LTE
Started	257	112	111
Completed	178	54	69
Not completed	79	58	42
Adverse event, serious fatal	2	1	2
Severe Non-compliance to Protocol	1	2	1
Condition Under Investigation Worsened	-	2	1
Failure to Meet Randomisation Criteria	-	-	1
Other - Not Due to COVID-19 Pandemic	2	6	2
Missing	1	-	-
Development of Study-specific Withdrawal Criteria	1	-	-
Consent withdrawn by subject	38	29	20
Adverse event, non-fatal	11	4	5
Lost to follow-up	5	6	3
Due to COVID-19 Pandemic	7	2	4
Condition Under Investigation Improved	1	-	-
Lack of efficacy	10	6	3

Number of subjects in period 1	Anifrolumab 150 mg Feeder +

	Anifrolumab 300 mg LTE
Started	67
Completed	41
Not completed	26
Adverse event, serious fatal	-
Severe Non-compliance to Protocol	-
Condition Under Investigation Worsened	-
Failure to Meet Randomisation Criteria	-
Other - Not Due to COVID-19 Pandemic	1
Missing	-
Development of Study-specific Withdrawal Criteria	1
Consent withdrawn by subject	12
Adverse event, non-fatal	8
Lost to follow-up	1
Due to COVID-19 Pandemic	-
Condition Under Investigation Improved	-
Lack of efficacy	3

Baseline characteristics

Reporting groups	
Reporting group title	Randomised Anifrolumab 300 mg
Reporting group description:	
Anifrolumab (300 mg) administered via an intravenous (IV) infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered anifrolumab (300 mg) in a feeder study.	
Reporting group title	Placebo Feeder + Placebo LTE
Reporting group description:	
Placebo administered via an IV infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered placebo in a feeder study.	
Reporting group title	Placebo Feeder + Anifrolumab 300 mg LTE
Reporting group description:	
Anifrolumab (300 mg) administered via an IV infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered placebo in a feeder study.	
Reporting group title	Anifrolumab 150 mg Feeder + Anifrolumab 300 mg LTE
Reporting group description:	
Anifrolumab (300 mg) administered via an IV infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered anifrolumab (150 mg) in a feeder study.	

Reporting group values	Randomised Anifrolumab 300 mg	Placebo Feeder + Placebo LTE	Placebo Feeder + Anifrolumab 300 mg LTE
Number of subjects	257	112	111
Age Categorical Units:			
<=18 years	0	0	0
Between 18 and 65 years	247	111	107
>=65 years	10	1	4
Age Continuous Units: Years			
arithmetic mean	43.4	41.4	42.2
standard deviation	± 11.51	± 11.46	± 12.24
Sex: Female, Male Units:			
Female	237	103	102
Male	20	9	9
Race Units: Subjects			
White	173	77	70
Black or African American	28	11	17
Asian	33	10	12
Native Hawaiian or Other Pacific Islander	0	0	0
American Indian or Alaska Native	3	1	0
Other	15	11	10
Missing	5	2	2
Ethnicity Units: Subjects			
Hispanic or Latino	54	28	22
Not Hispanic or Latino	198	82	87

Missing	5	2	2

Reporting group values	Anifrolumab 150 mg Feeder + Anifrolumab 300 mg LTE	Total	
Number of subjects	67	547	
Age Categorical Units:			
<=18 years	0	0	
Between 18 and 65 years	65	530	
>=65 years	2	17	
Age Continuous Units: Years			
arithmetic mean	42.4		
standard deviation	± 11.70	-	
Sex: Female, Male Units:			
Female	63	505	
Male	4	42	
Race Units: Subjects			
White	45	365	
Black or African American	10	66	
Asian	6	61	
Native Hawaiian or Other Pacific Islander	0	0	
American Indian or Alaska Native	0	4	
Other	6	42	
Missing	0	9	
Ethnicity Units: Subjects			
Hispanic or Latino	14	118	
Not Hispanic or Latino	53	420	
Missing	0	9	

End points

End points reporting groups

Reporting group title	Randomised Anifrolumab 300 mg
Reporting group description:	
Anifrolumab (300 mg) administered via an intravenous (IV) infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered anifrolumab (300 mg) in a feeder study.	
Reporting group title	Placebo Feeder + Placebo LTE
Reporting group description:	
Placebo administered via an IV infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered placebo in a feeder study.	
Reporting group title	Placebo Feeder + Anifrolumab 300 mg LTE
Reporting group description:	
Anifrolumab (300 mg) administered via an IV infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered placebo in a feeder study.	
Reporting group title	Anifrolumab 150 mg Feeder + Anifrolumab 300 mg LTE
Reporting group description:	
Anifrolumab (300 mg) administered via an IV infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered anifrolumab (150 mg) in a feeder study.	

Primary: Exposure-adjusted Incidence Rates (EAIRs) of Adverse Events of Special Interest (AESIs)

End point title	Exposure-adjusted Incidence Rates (EAIRs) of Adverse Events of Special Interest (AESIs)[1]
End point description:	
The event rate per 100 participant years was defined as the number of participants with an event divided by the sum of exposure time during the LTE study (including follow-up) in days for all participants in the analysis set multiplied by 365.25 days/year multiplied by 100. The exposure in a time period for each participant was calculated as end of period - start of period + 1. EAIRs of AESIs are presented as event rate per 100 participant years. The following AESIs were pre-defined: - Non-opportunistic serious infections - Opportunistic infections - Anaphylaxis - Malignancy - Herpes zoster - Tuberculosis (TB) (including latent TB) - Influenza - Vasculitis (non-systemic lupus erythematosus [SLE]) - Major cardiovascular events as according to the Cardiovascular Event Adjudication Committee. Full analysis set (FAS) - LTE Study: consist of all participants who were randomised and received at least 1 dose of investigational product in the LTE Study.	
End point type	Primary
End point timeframe:	
Up to a maximum of 1114 days	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No additional statistical analysis was pre-specified for this end point.	

End point values	Randomised Anifrolumab 300 mg	Placebo Feeder + Placebo LTE	Placebo Feeder + Anifrolumab 300 mg LTE	Anifrolumab 150 mg Feeder + Anifrolumab 300 mg LTE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	257	112	111	67
Units: Events per 100 participant years				
number (not applicable)	11.0	9.6	12.9	12.5

Statistical analyses

No statistical analyses for this end point

Primary: EAIRs of Serious Adverse Events (SAEs)

End point title	EAIRs of Serious Adverse Events (SAEs)[2]

End point description:

EAIRs of SAEs are presented as event rate per 100 participant years.
An SAE was an AE occurring during any study phase that fulfils 1 or more of the following criteria:
- Results in death
- Is immediately life-threatening
- Requires in-patient hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions
- Is a congenital abnormality or birth defect
- Is an important medical event that may jeopardise the participant or may require medical intervention to prevent one of the outcomes listed above.

FAS - LTE Study: consist of all participants who were randomised and received at least 1 dose of investigational product in the LTE Study.

End point type	Primary

End point timeframe:

Up to a maximum of 1114 days

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No additional statistical analysis was pre-specified for this end point.

End point values	Randomised Anifrolumab 300 mg	Placebo Feeder + Placebo LTE	Placebo Feeder + Anifrolumab 300 mg LTE	Anifrolumab 150 mg Feeder + Anifrolumab 300 mg LTE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	257	112	111	67
Units: Events per 100 participant years				
number (not applicable)	8.5	11.2	10.1	10.7

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 up to until follow-up visit 2 (Week 164)	
Adverse event reporting additional description:	
FAS - LTE Study: consist of all participants who were randomised and received at least 1 dose of investigational product in the LTE Study.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	Randomised Anifrolumab 300 mg
Reporting group description:	
Anifrolumab (300 mg) administered via an IV infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered anifrolumab (300 mg) in a feeder study.	
Reporting group title	Placebo Feeder + Placebo LTE
Reporting group description:	
Placebo administered via an IV infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered placebo in a feeder study.	
Reporting group title	Placebo Feeder + Anifrolumab 300 mg LTE
Reporting group description:	
Anifrolumab (300 mg) administered via an IV infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered placebo in a feeder study.	
Reporting group title	Anifrolumab 150 mg Feeder + Anifrolumab 300 mg LTE
Reporting group description:	
Anifrolumab (300 mg) administered via an IV infusion every 4 weeks for up to 152 weeks (39 doses). Participants were previously administered anifrolumab (150 mg) in a feeder study.	

Serious adverse events	Randomised Anifrolumab 300 mg	Placebo Feeder + Placebo LTE	Placebo Feeder + Anifrolumab 300 mg LTE
Total subjects affected by serious adverse events			
subjects affected / exposed	56 / 257 (21.79%)	27 / 112 (24.11%)	26 / 111 (23.42%)
number of deaths (all causes)	3	1	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	2 / 257 (0.78%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			

subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Malignant hypertension			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis limb			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	2 / 257 (0.78%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated hernia			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza like illness			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal haemorrhage			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical dysplasia			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heavy menstrual bleeding			

subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst ruptured			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine prolapse			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterovaginal prolapse			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 257 (0.39%)	1 / 112 (0.89%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			

subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Affect lability			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
International normalised ratio increased			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthropod bite			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periprocedural myocardial infarction			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rib fracture			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	2 / 257 (0.78%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve disease			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bundle branch block left			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 257 (0.39%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			

subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	2 / 257 (0.78%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post herpetic neuralgia			
subjects affected / exposed	2 / 257 (0.78%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial aneurysm			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system lupus			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	2 / 257 (0.78%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoperitoneum			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth impacted			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 257 (0.78%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Systemic lupus erythematosus			
subjects affected / exposed	6 / 257 (2.33%)	6 / 112 (5.36%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 6	0 / 8	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			

subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Herpes zoster			
subjects affected / exposed	6 / 257 (2.33%)	1 / 112 (0.89%)	3 / 111 (2.70%)
occurrences causally related to treatment / all	3 / 6	1 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	6 / 257 (2.33%)	2 / 112 (1.79%)	3 / 111 (2.70%)
occurrences causally related to treatment / all	0 / 6	1 / 2	0 / 3
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
COVID-19	Additional description: Only participants who were ongoing in the trial at the time the COVID-19 pandemic started are included. All participants who had completed or discontinued the trial prior to the pandemic are excluded from number of participants at risk.		
subjects affected / exposed[1]	4 / 201 (1.99%)	0 / 64 (0.00%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 2
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 1
COVID-19 pneumonia	Additional description: Only participants who were ongoing in the trial at the time the COVID-19 pandemic started are included. All participants who had completed or discontinued the trial prior to the pandemic are excluded from number of participants at risk.		

subjects affected / exposed[2]	3 / 201 (1.49%)	1 / 64 (1.56%)	3 / 82 (3.66%)
occurrences causally related to treatment / all	0 / 3	1 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyelonephritis			
subjects affected / exposed	3 / 257 (1.17%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 257 (0.78%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 257 (0.39%)	1 / 112 (0.89%)	2 / 111 (1.80%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster disseminated			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ophthalmic herpes zoster			

subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic inflammatory disease			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis streptococcal			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal urinary tract infection			
subjects affected / exposed	1 / 257 (0.39%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	2 / 111 (1.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis staphylococcal			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster meningitis			

subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected skin ulcer			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ludwig angina			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mediastinitis			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parotitis			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			

subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia staphylococcal			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative abscess			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection staphylococcal			
subjects affected / exposed	0 / 257 (0.00%)	1 / 112 (0.89%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 257 (0.00%)	0 / 112 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Anifrolumab 150 mg Feeder + Anifrolumab 300 mg LTE		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 67 (20.90%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thyroid cancer			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Malignant hypertension			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			

subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis limb				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pregnancy, puerperium and perinatal conditions				
Abortion spontaneous				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Non-cardiac chest pain				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest discomfort				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Incarcerated hernia				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza like illness				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Mucosal haemorrhage				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Uterine haemorrhage				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cervical dysplasia				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Heavy menstrual bleeding				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian cyst				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ovarian cyst ruptured				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Uterine prolapse				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterovaginal prolapse				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthma			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleurisy			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea exertional			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Respiratory distress			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Affect lability			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
International normalised ratio increased			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Overdose			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthropod bite			

subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Joint dislocation				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Periprocedural myocardial infarction				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural haemorrhage				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Myocardial ischaemia				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic valve disease				

subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bundle branch block left				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiogenic shock				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				

subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post herpetic neuralgia			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intracranial aneurysm			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Central nervous system lupus			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			

subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Iron deficiency anaemia			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemoperitoneum			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Inguinal hernia			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tooth impacted			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			

subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Systemic lupus erythematosus			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Arthritis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal stenosis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Synovial cyst			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tenosynovitis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			

Herpes zoster				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	3 / 67 (4.48%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			
COVID-19	Additional description: Only participants who were ongoing in the trial at the time the COVID-19 pandemic started are included. All participants who had completed or discontinued the trial prior to the pandemic are excluded from number of participants at risk.			
subjects affected / exposed[1]	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia	Additional description: Only participants who were ongoing in the trial at the time the COVID-19 pandemic started are included. All participants who had completed or discontinued the trial prior to the pandemic are excluded from number of participants at risk.			
subjects affected / exposed[2]	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dengue fever				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				

subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster disseminated				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ophthalmic herpes zoster				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic inflammatory disease				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis streptococcal				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Streptococcal urinary tract infection				

subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial sepsis				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis staphylococcal				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster meningitis				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infected skin ulcer				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ludwig angina				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mediastinitis				

subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Parotitis				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia influenzal				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia staphylococcal				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postoperative abscess				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Postoperative wound infection				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				

subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound infection staphylococcal			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Only participants who were ongoing in the trial at the time the COVID-19 pandemic started are included. All participants who had completed or discontinued the trial prior to the pandemic are excluded from number of participants at risk.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Only participants who were ongoing in the trial at the time the COVID-19 pandemic started are included. All participants who had completed or discontinued the trial prior to the pandemic are excluded from number of participants at risk.

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Randomised Anifrolumab 300 mg	Placebo Feeder + Placebo LTE	Placebo Feeder + Anifrolumab 300 mg LTE
Total subjects affected by non-serious adverse events			
subjects affected / exposed	195 / 257 (75.88%)	79 / 112 (70.54%)	81 / 111 (72.97%)
Injury, poisoning and procedural complications			
Infusion related reaction			

subjects affected / exposed	17 / 257 (6.61%)	6 / 112 (5.36%)	8 / 111 (7.21%)
occurrences (all)	28	10	13
Fall			
subjects affected / exposed	11 / 257 (4.28%)	6 / 112 (5.36%)	4 / 111 (3.60%)
occurrences (all)	15	8	5
Contusion			
subjects affected / exposed	10 / 257 (3.89%)	3 / 112 (2.68%)	7 / 111 (6.31%)
occurrences (all)	12	3	8
Vascular disorders			
Hypertension			
subjects affected / exposed	13 / 257 (5.06%)	4 / 112 (3.57%)	4 / 111 (3.60%)
occurrences (all)	17	4	4
Nervous system disorders			
Headache			
subjects affected / exposed	28 / 257 (10.89%)	11 / 112 (9.82%)	7 / 111 (6.31%)
occurrences (all)	35	14	13
Dizziness			
subjects affected / exposed	8 / 257 (3.11%)	3 / 112 (2.68%)	4 / 111 (3.60%)
occurrences (all)	9	3	6
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	18 / 257 (7.00%)	6 / 112 (5.36%)	8 / 111 (7.21%)
occurrences (all)	21	7	9
Nausea			
subjects affected / exposed	12 / 257 (4.67%)	7 / 112 (6.25%)	6 / 111 (5.41%)
occurrences (all)	16	8	9
Abdominal pain upper			
subjects affected / exposed	7 / 257 (2.72%)	2 / 112 (1.79%)	5 / 111 (4.50%)
occurrences (all)	7	2	6
Constipation			
subjects affected / exposed	7 / 257 (2.72%)	7 / 112 (6.25%)	3 / 111 (2.70%)
occurrences (all)	7	9	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	18 / 257 (7.00%)	4 / 112 (3.57%)	4 / 111 (3.60%)
occurrences (all)	19	4	4

Psychiatric disorders			
Depression			
subjects affected / exposed	9 / 257 (3.50%)	4 / 112 (3.57%)	3 / 111 (2.70%)
occurrences (all)	9	4	3
Insomnia			
subjects affected / exposed	8 / 257 (3.11%)	3 / 112 (2.68%)	5 / 111 (4.50%)
occurrences (all)	9	3	7
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	21 / 257 (8.17%)	9 / 112 (8.04%)	11 / 111 (9.91%)
occurrences (all)	28	10	13
Back pain			
subjects affected / exposed	18 / 257 (7.00%)	10 / 112 (8.93%)	12 / 111 (10.81%)
occurrences (all)	21	12	15
Systemic lupus erythematosus			
subjects affected / exposed	12 / 257 (4.67%)	2 / 112 (1.79%)	3 / 111 (2.70%)
occurrences (all)	17	2	3
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	57 / 257 (22.18%)	16 / 112 (14.29%)	18 / 111 (16.22%)
occurrences (all)	71	21	27
Nasopharyngitis			
subjects affected / exposed	63 / 257 (24.51%)	13 / 112 (11.61%)	29 / 111 (26.13%)
occurrences (all)	139	33	48
Upper respiratory tract infection			
subjects affected / exposed	55 / 257 (21.40%)	18 / 112 (16.07%)	22 / 111 (19.82%)
occurrences (all)	95	24	41
Bronchitis			
subjects affected / exposed	41 / 257 (15.95%)	9 / 112 (8.04%)	17 / 111 (15.32%)
occurrences (all)	56	9	24
Pharyngitis			
subjects affected / exposed	20 / 257 (7.78%)	5 / 112 (4.46%)	12 / 111 (10.81%)
occurrences (all)	29	5	18
Sinusitis			
subjects affected / exposed	24 / 257 (9.34%)	3 / 112 (2.68%)	9 / 111 (8.11%)
occurrences (all)	29	3	15

Oral herpes			
subjects affected / exposed	19 / 257 (7.39%)	6 / 112 (5.36%)	6 / 111 (5.41%)
occurrences (all)	33	8	8
Herpes zoster			
subjects affected / exposed	16 / 257 (6.23%)	6 / 112 (5.36%)	12 / 111 (10.81%)
occurrences (all)	18	6	12
Latent tuberculosis			
subjects affected / exposed	16 / 257 (6.23%)	2 / 112 (1.79%)	4 / 111 (3.60%)
occurrences (all)	16	2	4
Influenza			
subjects affected / exposed	14 / 257 (5.45%)	5 / 112 (4.46%)	9 / 111 (8.11%)
occurrences (all)	14	5	9
Gastroenteritis			
subjects affected / exposed	7 / 257 (2.72%)	7 / 112 (6.25%)	13 / 111 (11.71%)
occurrences (all)	9	9	17

Non-serious adverse events	Anifrolumab 150 mg Feeder + Anifrolumab 300 mg LTE		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 67 (79.10%)		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences (all)	9		
Fall			
subjects affected / exposed	3 / 67 (4.48%)		
occurrences (all)	5		
Contusion			
subjects affected / exposed	6 / 67 (8.96%)		
occurrences (all)	8		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 67 (4.48%)		
occurrences (all)	5		
Nervous system disorders			

Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	 10 / 67 (14.93%) 11 4 / 67 (5.97%) 4		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	 5 / 67 (7.46%) 11 2 / 67 (2.99%) 2 4 / 67 (5.97%) 4 0 / 67 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 7 / 67 (10.45%) 9		
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	 4 / 67 (5.97%) 4 7 / 67 (10.45%) 7		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain	 3 / 67 (4.48%) 6 		

subjects affected / exposed	9 / 67 (13.43%)		
occurrences (all)	12		
Systemic lupus erythematosus			
subjects affected / exposed	5 / 67 (7.46%)		
occurrences (all)	6		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	9 / 67 (13.43%)		
occurrences (all)	12		
Nasopharyngitis			
subjects affected / exposed	15 / 67 (22.39%)		
occurrences (all)	24		
Upper respiratory tract infection			
subjects affected / exposed	8 / 67 (11.94%)		
occurrences (all)	14		
Bronchitis			
subjects affected / exposed	16 / 67 (23.88%)		
occurrences (all)	19		
Pharyngitis			
subjects affected / exposed	9 / 67 (13.43%)		
occurrences (all)	11		
Sinusitis			
subjects affected / exposed	6 / 67 (8.96%)		
occurrences (all)	7		
Oral herpes			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	10 / 67 (14.93%)		
occurrences (all)	10		
Latent tuberculosis			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	5 / 67 (7.46%)		
occurrences (all)	5		

Gastroenteritis subjects affected / exposed occurrences (all)	3 / 67 (4.48%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 May 2016	- Removed requirement that female participants with an intact cervix must have documentation of a Pap smear with no documented malignancy before Day 1/Visit 1 and yearly thereafter. - Previous use (within the last 60 days) of mizoribine > 150 mg/day has been added as an exclusion criterion. - Added requirement that human immunodeficiency virus status must be confirmed by a test performed by the central laboratory if not tested in feeder studies.
10 August 2017	- Added requirement that females with an intact cervix must have a Pap smear without documented malignancy. Added that all female participants with an intact cervix should have a Pap smear performed within 3 months of the last investigational product dose, e.g., at the end of study or at the early discontinuation. visit. - The requirement for QuantiFERON® (QFT) testing for cases where newly indeterminate QFT test results are obtained was added. The QFT testing for tuberculosis was added to the list of assessments to be performed at the Early Discontinuation Visit. - Mizoribine was added to the list of permitted immunosuppressants. - Mycophenolic acid was added to the list of permitted immunosuppressants in the Protocol synopsis and the dose of mycophenolic acid not to be exceeded was updated to > 1.44 g/day. - Baricitinib, tofacitinib, or other Janus kinase inhibitors were added to the list of prohibited concomitant medications. - Updates were made to the permitted and prohibited medications. Topical retinoids were removed from the list of prohibited medications. - Serum chemistry, haematology and urinalysis sampling were added to Visit 3/Week 8 and Visit 10/Week 36.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported